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The Signal-Averaged P Wave Duration: A Rapid and Noninvasive Marker of Risk of Atrial Fibrillation

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Objectives. This study was undertaken to determine the ability of the signal-averaged electrocardiogram (ECG) to identify evidence of delayed atrial activation in patients with a history of atrial fibrillation.

Background. Atrial fibrillation is a reentrant rhythm and depends on atrial conduction delay for its development. The signal-averaging technique is useful for accurately measuring total cardiac activation times, including delayed low amplitude signals, and thus can help identify the substrate for reentrant arrhythmias.

Methods. Standard 12-lead and signal-averaged ECGs were recorded from 15 patients with a documented history of prior paroxysmal or chronic atrial fibrillation and 15 age- and disease-matched control subjects without a history of atrial fibrillation. Signal averaging was performed using an orthogonal lead system with the QRS complex as a trigger and the P wave as a template for the signal-averaging process. Total P wave duration was measured before and after filtering with a least squares fit filter. The P wave complexes on the three bipolar leads were combined into a vector combination of orthogonal leads. The total P wave duration of the individual unfiltered and filtered leads and the vector combination of filtered leads were calculated and used for analysis.

Results. The P wave duration by standard ECG was not significantly different in patients with a history of atrial fibrillation and control subjects. Signal-averaged P wave durations were measured from orthogonal leads before and after digital filtering. Mean unfiltered P wave duration was significantly longer in patients with a history of atrial fibrillation than in control subjects (132 ± 22 vs. 114 ± 14 ms [$p < 0.03$] in the X lead, 135 ± 21 vs. 115 ± 15 ms [$p < 0.03$] in the Y lead and 133 ± 23 vs. 114 ± 14 ms [$p < 0.03$] in the Z lead). Mean filtered P wave duration was also longer in patients with atrial fibrillation than in control subjects (151 ± 23 vs. 130 ± 19 ms [$p < 0.01$] in the X lead, 157 ± 22 vs. 136 ± 17 ms [$p < 0.01$] in the Y lead and 154 ± 23 vs. 135 ± 15 ms [$p < 0.01$] in the Z lead). After filtering, a vector composite of orthogonal leads was determined. Again, P wave duration in patients with a history of atrial fibrillation exceeded that in the control subjects (162 ± 15 vs. 140 ± 12 ms [$p < 0.01$]). Using the vector composite of filtered orthogonal leads, a P wave duration ≥155 ms was associated with a sensitivity of 80%, a specificity of 93% and a positive predictive value of 92% for identifying patients with history of atrial fibrillation.

Conclusions. A prolonged signal-averaged P wave duration may be a simple noninvasive marker of the risk for development of atrial fibrillation.

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Over the past decade, the signal-averaged electrocardiogram (ECG) has emerged as an increasingly valuable tool in the evaluation of patients with known or suspected ventricular arrhythmias. Simson (1) initially described the presence of late potentials in the terminal portion of the signal-averaged QRS complex in patients with sustained ventricular tachycardia after myocardial infarction. Late potentials correspond in time with delayed cardiac activation and are believed to indicate the existence of a substrate for reentrant ventricular arrhythmias (2–5). The presence of QRS late potentials has also been shown to be predictive of both electrically inducible ventricular tachycardia at electrophysiologic study (6–8) and arrhythmic events after myocardial infarction (5).

Although the discovery of QRS late potentials has led to important clinical applications of the signal-averaged ECG with respect to ventricular tachyarrhythmias, investigators (9–12) have only recently attempted to study the signal-averaged P wave and its relation to atrial arrhythmia. Analogous to ventricular tachycardia, atrial fibrillation is thought to be due to reentrant mechanisms and thus the atria require areas of slow conduction to initiate and maintain the reentrant circuit (13–15). We therefore hypothesized that the signal-averaged ECG, by attenuating body surface noise, would have the sensitivity to detect delayed atrial activation in patients with a history of atrial fibrillation.

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The purpose of this study was to employ a signal-averaging process using P wave template matching to measure total atrial activation and test the hypothesis that atrial activation is prolonged in patients with a history of atrial fibrillation compared with that in age- and disease-matched control subjects.

Methods

Patient selection. The study was approved by the Institutional Review Board of our medical center. Informed consent was obtained from all patients. The study enrolled two groups of hospitalized patients at the center. Patients with a documented history of chronic or paroxysmal atrial fibrillation were consecutively identified on the medical service and were considered eligible for this study if the rhythm at the time of signal-averaged ECG recording was normal sinus rhythm. Patients receiving class I antiarrhythmic agents were excluded because these agents prolong atrial conduction. A control group was selected from hospitalized patients with no history of paroxysmal or chronic atrial fibrillation, who were then matched with the study group for age and underlying heart disease.

Signal-averaged ECG methodology. The signal-averaged ECG was recorded with the Predictor system (Corazonix Corporation). The subject's skin was cleansed with alcohol and abraded with gauze. An orthogonal lead arrangement was used (identical to that in conventional signal-averaged ECG recording). Three electrode pairs were placed in the following locations: 1) X, at the fourth intercostal space in both midaxillary lines; 2) Y, in the midclavicular line just inferior to the clavicle and to the left of the umbilicus; and 3) Z, in the fourth intercostal space to the left of the sternum and the vertebral column. Positive electrodes were left, anterior and inferior. The electrodes used were silver/silver chloride. The QRS complex was used as the trigger for the signal-averaging process; the fiducial point was, however, shifted to the extreme right side of the 300-ms window to expose the P wave and the PR segment. The signal was digitized at a frequency of 2,000 samples/s with 16-bit accuracy. This system utilized a cross-correlation program; a sinus P wave template was selected by the operator and P wave complexes that did not match the template with a 99% correlation coefficient were automatically rejected. Rejected P waves included atrial ectopic beats, excessively noisy sinus beats and sinus beats that did not match the template because of slight fluctuations in the PR interval occurring as a consequence of changes in autonomic tone. The correlation window width was 25 ms and the number of correlations to achieve a fit was 10. The P wave complexes were acquired until a noise end point <0.3 μV in the TP segment was achieved. This template-matching process ensured acceptance of accurately aligned sinus P waves and rejection of ectopic P waves or misaligned sinus P waves (± 0.5-ms jitter). The mean number of beats averaged to achieve a noise end point <0.3 μV was 262 ± 204 (range 84 to 549) in patients with atrial fibrillation and 282 ± 169 (range 105 to 842) in control subjects (p = NS).

A least squares fit filter with a window width of 100 ms (giving an equivalent high pass cutoff of 29 Hz) was applied to the averaged output and the result amplified to improve visualization of the low amplitude components. The least squares fit filter operates by fitting a smooth curve to each segment of predefined length of the ECG. The fitted curve is subtracted from the original waveform to leave a residual or high pass portion of the ECG signal. The length of the segment or window can be adjusted; a shorter segment leaves a smaller residual effectively increasing the high pass cutoff frequency of the filter. The detailed characteristics of the least squares fit filter have been described elsewhere (16). The P wave complexes of the three bipolar leads were combined into a vector magnitude by the formula $\sqrt{(X^2+Y^2+Z^2)}$. The P wave onset and offset were determined manually and performed without knowledge of the patient's arrhythmia status. The P wave onset was the first atrial deflection from the baseline noise level and the offset was the return of the atrial signal to the baseline or onset of the QRS complex, whichever was earlier. The total P wave duration of the individual unfiltered and filtered X, Y and Z leads and the vector combination of filtered leads were calculated and used for analysis. We chose to measure total P wave duration only rather than, or in addition to, calculation of terminal segment amplitude. The decision to measure only total P wave duration was based on prior experience with QRS signal averaging, where QRS duration (rather than terminal QRS measurements) is the measurement most closely correlated with abnormal conduction and arrhythmia risk (5,17–19), the concern that terminal voltage measurements are poorly reproducible (20) and the absence of any nonarbitrary position to divide the P wave that would be predicted to correlate accurately with delayed atrial activation.

Standard ECG methodology. A standard 12-lead ECG recorded within 24 h of the signal-averaged ECG was reviewed for each patient. All standard ECGs were obtained at a paper speed of 25mm/s and a signal size of 10 mm/mV. Standard ECG analysis was performed without knowledge of the patient's clinical status. Total P wave durations in all limb leads were manually measured and the longest limb lead P wave duration was recorded and used for analysis. A P wave duration on the standard ECG >110 ms was considered abnormal (21).

Statistical analyses. Results were expressed as group mean ± SD. Comparisons between groups were made with the Student *t* test for paired and unpaired data. A p value < 0.05 was considered significant.

Results

Study patients. The study group consisted of 15 patients with a prior history of atrial fibrillation (paroxysmal in 10 patients and chronic in 5). Fifteen age- and disease-matched

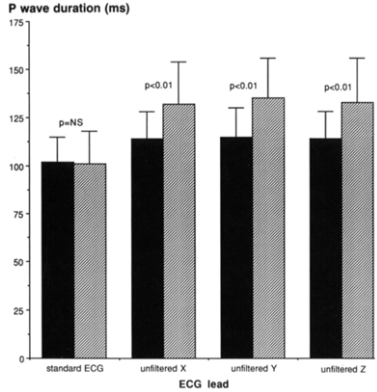


Figure 1. P wave duration as measured by standard and unfiltered signal-averaged electrocardiogram (ECG). The mean (± SD) P wave duration for 15 patients with atrial fibrillation **(hatched bars)** and 15 control subjects **(black bars)** are shown. The difference in P wave duration between the two groups is not statistically significant as measured by standard ECG but P wave duration as measured by signal-averaged ECG is significantly prolonged in the X, Y and Z leads in patients with atrial fibrillation relative to that in control subjects.

patients with no known history of atrial fibrillation served as control subjects. The mean age was 68 ± 14 years in the atrial fibrillation group and 62 ± 16 years in the control group (p = NS). All patients had normal sinus rhythm at the time of study. The five patients with a history of chronic atrial fibrillation had recently undergone electrical cardioversion and at the time of study, two of these patients were receiving dl-sotalol, an investigational class III antiarrhythmic agent with no known effect on atrial conduction (22). No other patients in either group were receiving antiarrhythmic medication and no patient had a history of receiving amiodarone. Nine patients in the atrial fibrillation group and eight patients in the control group had underlying hypertensive heart disease, and five patients in each group had ischemic heart disease. Four patients in each group had no known underlying heart disease.

P wave duration on the standard 12-lead ECG. In the atrial fibrillation group, the P wave duration measured by standard ECG ranged from 60 to 120 ms (mean 101 ± 17). In the control group, P wave duration by standard ECG ranged from 80 to 120 ms (mean 102 ± 13) (Fig. 1). Three patients in each group had a P wave duration >110 ms.

Unfiltered and filtered signal-averaged P wave duration. Data summarizing the unfiltered P wave duration for each orthogonal lead of the signal-averaged ECG for control and subjects and patients with atrial fibrillation are shown in Figure 1. As a result of amplification and noise reduction, unfiltered P wave duration after signal averaging was significantly longer than P wave duration measured on the standard ECG in both groups. In the patients with atrial fibrillation, mean P wave duration increased after signal averaging in each of the three orthogonal leads from 101 ± 17 ms to 132 ± 22 ($p < 0.01$), 135 ± 21 ($p < 0.01$) and 133 ± 23 ms ($p < 0.01$) in the X, Y and Z leads, respectively. The P wave duration after signal averaging increased in the control group from 102 ± 13 ms to 114 ± 14 ($p < 0.01$), 115 ± 15 ($p < 0.01$) and 114 ± 14 ms ($p < 0.01$) in the X, Y and Z leads, respectively.

The effect of filtering was an increase in measured P wave duration relative to unfiltered P wave duration in both groups because of amplification and enhanced detection of low amplitude signals. We cannot entirely exclude the possibility that the least squares filter caused some prolongation. The mean P wave duration in patients with atrial fibrillation increased from 132 ± 22 ms to 151 ± 23 ms ($p < 0.01$), from 135 ± 21 to 157 ± 22 ms ($p < 0.01$) and from 133 ± 23 to 154 ± 23 ms ($p < 0.01$) in the X, Y and Z leads, respectively. In the control group, P wave duration increased after filtering from 114 ± 14 to 130 ± 19 ms ($p < 0.01$) in the X lead, from 115 ± 15 to 136 ± 17 ms ($p < 0.01$) in the Y lead and from 114 ± 14 to 135 ± 15 ms ($p < 0.01$) in the Z lead.

Signal-averaged P wave duration in the two groups. In each of the orthogonal leads, the unfiltered P wave duration was significantly longer in the patients with a history of atrial fibrillation than in the matched control subjects. In each lead, the mean unfiltered P wave duration in the atrial fibrillation group exceeded the mean unfiltered P wave duration in the control group (132 ± 22 vs. 114 ± 14 ms [$p < 0.03$] in the X lead, 135 ± 21 vs. 115 ± 15 ms [$p < 0.03$] in the Y lead and 133 ± 23 vs. 114 ± 14 ms [$p < 0.03$] in the Z lead [Fig. 1]). Within both the atrial fibrillation and control groups, there was no significant difference in P wave duration as measured in each of the three orthogonal leads.

Filtered P wave duration was longer in patients with atrial fibrillation than in the control group (mean 151 ± 23 vs. 130 ± 19 ms [$p < 0.01$] in the X lead, 157 ± 22 vs. 136 ± 17 ms [$p < 0.01$] in the Y lead and 154 ± 23 vs. 135 ± 15 ms [$p < 0.01$] in the Z lead [Fig. 2]). Within each group, there was no significant difference in P wave duration as measured in each of the three orthogonal leads.

The three orthogonal leads were combined into a vector composite lead. Again, the mean P wave duration in the atrial fibrillation group was longer by 16% than that in the control group (162 ± 15 vs. 140 ± 12 ms [$p < 0.01$] [Fig. 2]). Examples of signal-averaged vector combinations of orthogonal leads are shown in Figure 3.

Sensitivity and specificity of P wave duration for atrial fibrillation. The P wave duration of the filtered vector composite leads for all patients with atrial fibrillation and control subjects was used to determine the sensitivity and specificity of P wave signal averaging for identifying patients with a

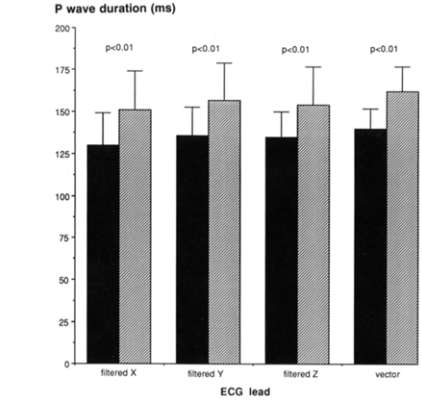


Figure 2. Mean ± SD P wave duration measured by signal-averaged electrocardiogram (ECG) in each of three orthogonal leads and their vector combination after filtering. There is significant P wave prolongation in the 15 patients with atrial fibrillation (**hatched bars**) relative to that in the 15 control subjects (**black bars**) in each individual lead and in the vector composite.

history of atrial fibrillation (Fig. 4). A P wave duration ≥155 ms yielded a sensitivity of 80% (12 of 15 patients), specificity of 93% (14 of 15 patients) and a positive predictive value of 92% (12 of 13 patients) for identifying patients with a history of atrial fibrillation.

Discussion

The association of QRS late potentials with ventricular tachycardia has allowed the signal-averaged ECG to play an increasingly important role in the noninvasive evaluation of a wide variety of patients at risk for ventricular arrhythmias. The potential uses of the signal-averaged ECG for evaluating patients with a propensity for atrial arrhythmias have not been adequately explored. Our results suggest that the signal-averaged ECG can be used to demonstrate prolonged atrial conduction not apparent on the standard ECG as a result of better detection of low amplitude signals in patients with a history of atrial fibrillation.

Using a system designed to analyze total atrial activation time, we found that the signal-averaged P wave duration was significantly longer in patients with prior atrial fibrillation than in age- and disease-matched control subjects. Signal-averaged P wave duration was prolonged in unfiltered orthogonal leads and filtered orthogonal and vector leads. Maximal differences that yielded a clinically useful separation between patients and control subjects were evident on the vector lead. The signal-averaging process utilized in this study allowed detection and accurate delineation of small atrial signals in the early and, more important, the late components of the P wave not apparent on the standard ECG.

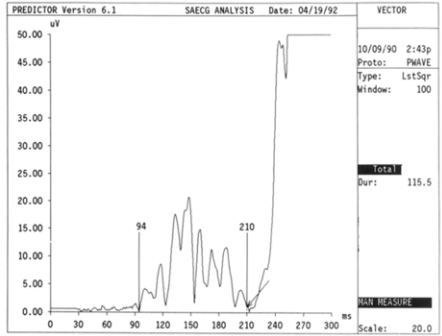
Study rationale. The mechanism of atrial fibrillation is thought to involve reentry. The model developed by Moe (14) for atrial fibrillation involving multiple wavelets of conduction produced by multiple atrial sites of rate-dependent conduction block has been confirmed by recording conduction patterns during induced episodes of atrial fibrillation in the canine model and in humans (13,15). Just as the presence of QRS late potentials indicates slowed conduction and the anatomic substrate for reentrant ventricular arrhythmias (23–25), a delay in atrial conduction measured on the signal-averaged ECG may reveal the physiologic substrate for atrial fibrillation.

The process of signal averaging attenuates electrical noise and facilitates detection of low amplitude signals such as those reflecting regions of delayed myocardial activation. It was our hypothesis that P wave signal averaging would provide a rapid noninvasive method of identifying atrial conduction delay.

Atrial fibrillation is most commonly seen in patients with underlying structural heart disease, including hypertensive heart disease, rheumatic valvular disease, coronary artery disease, pulmonary embolism and pericardial disease. Although these clinical states identify patients at increased risk for the development of atrial fibrillation, there is no reliable method for stratifying the relative risk of developing atrial fibrillation within this large group of patients. Because the development of atrial fibrillation is associated with a significantly increased risk of morbidity and mortality, a means of identifying these patients well before the onset of atrial fibrillation could lead to more frequent surveillance of these patients and possibly a more aggressive approach to the treatment of their underlying cardiovascular disorder or a prophylactic intervention for atrial fibrillation. Even if it were not possible to avert the onset of atrial fibrillation, therapeutic strategies could be tailored to minimize the associated morbidity.

Previous studies using the standard ECG. In an attempt to identify a subset of patients at particularly high risk for developing atrial fibrillation or flutter after aortocoronary bypass grafting, Buxton and Josephson (26) observed the postoperative course of 99 patients undergoing this operation. The presence of an intraatrial conduction defect did not identify patients at risk for postoperative atrial fibrillation or flutter. These investigators were able to derive a predictor of postoperative atrial fibrillation or flutter by measuring total P wave duration obtained from the simultaneous recording of the three standard limb leads, but the poor specificity limited the usefulness of this technique.

P wave analysis using the signal-averaged ECG. A major obstacle to the application of signal averaging to the study of atrial arrhythmias has been the variable temporal relation



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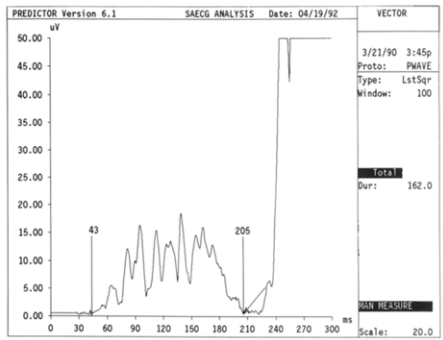

B

Figure 3. Examples of measured P waves from the vector combination of filtered orthogonal leads. **A**, Signal-averaged electrocardiogram (SAECG) from a control subject with a measured P wave duration (Dur) of 116 ms. **B**, Recording from a patient with atrial fibrillation who had a P wave duration of 162 ms. LstSqr = least squares fit filter; Proto = protocol.

between atrial and ventricular depolarization. This variability is influenced by changes in autonomic tone due to respiration, and it results in slight fluctuations in the PR interval over time. The commonly used signal-averaging method is a temporal process that utilizes the QRS complex as the reference point or trigger, and as the template for acceptance or rejection during the signal-averaging acquisition. Although acceptable for measurement of the QRS complex, this method of signal averaging is not optimal for analysis of the P wave because the variability of the PR interval (and thus the relation of the P wave to the QRS complex) over the course of the signal-averaged acquisition causes an unacceptable amount of jitter, making interpretation and detection of high frequency signals of the P wave unreliable. We modified the conventional signal-averaging process on a commercially available system by retaining the QRS complex as the trigger but using the P wave as the template. Using this method, all P waves that did not match the exact timing of the selected template were rejected and proper alignment was ensured, thereby reducing jitter to ±0.5 ms. Extremely accurate alignment was achieved with a cross-correlation function that required a coefficient of 0.99. In addition, the filter applied to the signal-averaged P wave was designed to limit any signal distortion or oscillation that can result from the bidirectional filtering commonly used for QRS signal averaging if it is centered at the QRS complex. The least squares fit filter is a high pass digital filter with a linear phase response. It markedly diminishes ringing compared with unidirectional filters and will not carry any QRS energy into the P wave.

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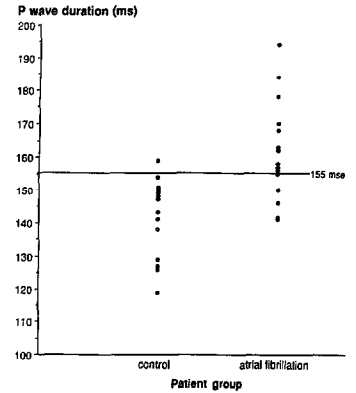

Figure 4. The P wave duration of vector combination of filtered orthogonal leads for all 15 patients with atrial fibrillation and the 15 control subjects. A P wave duration ≥155 ms identified patients with a history of atrial fibrillation with a sensitivity of 80% and a specificity of 93%.

Initial study. In the first reported attempt to signal average P waves, Engel et al. (9) compared P wave durations in three groups: normal subjects, patients with a history of paroxysmal or recently converted atrial fibrillation and control patients with a history of sustained ventricular tachycardia, congestive heart failure or acute myocardial infarction. These investigators attempted to identify low amplitude atrial signals by subtracting unfiltered from filtered P wave duration. Although the filtered P wave duration was prolonged in comparison with the value in normal subjects, it was not longer in the atrial fibrillation group than in the control group. Filtered minus unfiltered P wave duration was not significantly different in any of the three groups, leading the investigators to conclude that the signal-averaged ECG was not helpful in identifying patients with a history of atrial fibrillation. The limitations in this initial attempt to signal average P waves were acknowledged by Engel (10) in a subsequent review of the signal-averaged ECG. In addition to the previously mentioned differences in signal-averaging methodology (use of the P wave rather than the QRS complex as a template and use of a least squares rather than a bidirectional filter to eliminate distortion of the P wave), differences in patient selection may have contributed to the contrast between our results and those reported by Engel et al. (9). Specifically, we excluded patients receiving class I antiarrhythmic agents (which are known to prolong atrial activation) and selected a control group that was matched for age and underlying heart disease.

Later studies. More recently, Fukunami et al. (11) reported success in using the signal-averaged ECG to identify patients at risk for atrial fibrillation. These investigators recorded signal-averaged ECGs from a group of patients with paroxysmal atrial fibrillation and a group of age- and disease-matched control patients using a custom-designed P wave–triggered signal-averaging system. There were significant differences in the measured signal-averaged P wave variables, including total P wave duration between the atrial fibrillation and control groups. However, excessive overlap between patients and control subjects limited the clinical utility of the findings reported in their study. The methodology used by these investigators differs significantly from that used in our study. Because their method of P wave filtering utilized an analog unidirectional filter, it is possible that some P wave durations could have been extended by a filter-ringing artifact. Furthermore, their method of P wave correlation was not reported. It is unclear whether better filtering or improved correlation, or both, would have enhanced the separation of signal-averaged P wave duration between the atrial fibrillation and control groups.

Stafford et al. (12) found that signal-averaged P wave duration was significantly but minimally longer in 9 patients with paroxysmal atrial fibrillation than in 15 age-matched control subjects. However, when the data were dichotomized, signal-averaged P wave duration did not distinguish between the two groups. Although these investigators used the P wave as a template, correlations were made visually, it is therefore possible that inadequate correlation might have increased jitter, thus limiting the detection of high frequency atrial signals and creating greater overlap between patients with atrial fibrillation and control subjects.

Limitations of the present study. This present investigation has several limitations. 1) Although none of the patients with atrial fibrillation had recently received class I antiarrhythmic drugs and none had ever received amiodarone, two patients were receiving the class III drug dl-sotalol. However, dl-sotalol has no known effects on atrial conduction (22) and thus should not have altered our findings. When the two patients who were receiving dl-sotalol and their age- and disease-matched control subjects were excluded from data analysis, the results were unchanged. 2) Patients with paroxysmal atrial fibrillation were grouped with patients with chronic atrial fibrillation who had recently undergone electrical cardioversion. Although these are not identical patient groups, a previous investigation (27) has shown that these patients share similar electrophysiologic abnormalities, as determined by direct cardiac recordings. 3) Intracardiac recordings were not available to correlate atrial activation times with the signal-averaged P wave measurements. Although the increased P wave duration seen in both patient groups after filtering was attributed to amplification and detection of low amplitude atrial signals, we cannot exclude the possibility that the least squares filter itself caused some increase in the measured P wave duration by spreading the signal. 4) The number of patients studied was relatively

small. 5) Echocardiographic data to correlate atrial dimension with measured standard and signal-averaged ECG data were not available.

Conclusions. In the present study, the signal-averaged P wave duration was longer in patients with prior chronic or paroxysmal atrial fibrillation than in age- and disease-matched control subjects. Delayed atrial conduction in patients with a history of atrial fibrillation was not evident on the standard 12-lead ECG. A signal-averaged P wave duration ≥155 ms had good sensitivity and excellent specificity for identifying patients with a history of atrial fibrillation. Our results suggest that the signal-averaged ECG P wave duration is a simple and rapid noninvasive method obtainable with commercially available signal-averaging systems. This method merits further prospective study in large patient groups to determine its clinical role in identifying patients at risk for developing atrial fibrillation.

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